AB0801

EFFECTS OF GUSELKUMAB, A MONOCLONAL ANTIBODY THAT SPECIFICALLY BINDS TO THE P19-SUBUNIT OF INTERLEUKIN-23, ON DACTYLITIS AND ENTHESITIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: POOLED RESULTS THROUGH WEEK 24 FROM TWO PHASE 3 STUDIES

D. McGonagle¹, I. McInnes², A. Deodhar³, G. Schett⁴, P. J. Mease⁵, M. Shawi⁶, S. Kafka⁷, C. Karyekar⁸, A. Kollmeier⁹, E. C. Hsia^{8,9}, X. L. Xu⁸, S. Sheng⁸, P. Agarwal⁸, B. Zhou⁸, C. T. Ritchlin¹⁰, P. Rahman¹¹. ¹Leeds Biomed Res Ctr, U Leeds, Leeds, United Kingdom; ²U Glasgow, Glasgow, United Kingdom; ³Oregon Health & Science U, Portland, United States of America; ⁴FAU, Erlangen-Nürnberg, Germany; ⁵Swedish Med Ctr/ Providence St Joseph Health and U Wash School of Med, Seattle, United States of America; ⁶Janssen Global Svcs, LLC, Horsham, United States of America; ⁷Janssen Scientific Affairs, LLC, Horsham, United States of America; ⁸Janssen Research & Development, LLC, Spring House, United States of America; ⁹U Penn Med Ctr, Philadelphia, United States of America; ¹⁰U Rochester Med Center, Rochester, United States of America; ¹¹Memorial U Newfoundland, St. Johns, Canada

Background: Guselkumab (GUS), a novel monoclonal antibody that specifically binds to the p19-subunit of IL-23, demonstrated efficacy in the Ph 3 DISCOVER-1 (D1) & DISCOVER-2 (D2) trials of pts with active psoriatic arthritis (PsA).^{1,2} Dactylitis & enthesitis, key PsA clinical manifestations, can be difficult to treat and may portend more significant disease burden.^{3,4}

Objectives: In pts with dactylitis or enthesitis at baseline, assess: 1) changes in symptoms over time and 2) relationships between improvements in dactylitis or enthesitis and other PsA domains.

Methods: Adults with active PsA despite standard therapies were eligible for D1 & D2. Approx. 30% of D1 pts previously received 1-2 TNF inhibitors; D2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100mg Q4W; GUS 100mg at W0, W4, Q8W; or PBO. Independent assessors evaluated dactylitis (total score: 0-60) & enthesitis (Leeds Enthesitis Index [LEI]; total score 0-6). Dactylitis and enthesitis findings through W24 were prespecified to be pooled across D1 & D2. P-values are unadjusted. We assessed changes in dactylitis and LEI scores over time (ANCOVA); associations between dactylitis or enthesitis resolution and ACR/PASI responses at W24 (Chi-square); and correlations between dactylitis or LEI and HAQ-DI/SF-36 change scores at W24 (Spearman's correlation). AEs through W24 were reported.^{1,2}

Results: At W0, 42% of pooled D1+D2 pts had dactylitis; 65% had enthesitis. GUS improved dactylitis and LEI scores vs PBO at W8, W16, W24. GUS vs PBO differences were significant for dactylitis changes at W16 & W24 and LEI changes at W8 (Q4W only), W16 & W24; no dose response was observed (Fig). Rates of dactylitis or enthesitis resolution by W24 were consistently significantly ($p < 0.001$) associated with ACR20/50/70 and PASI75/90 response (Table). In GUS-treated pts at W24, significant correlations were observed between dactylitis change scores and PASI ($p < 0.001$ Q4W; $p = 0.006$ Q8W) and SF-36 MCS ($p = 0.038$ Q4W; $p = 0.003$ Q8W) changes, and between LEI and HAQ-DI change scores ($p < 0.001$ Q4W; $p = 0.005$ Q8W). No consistent correlations/associations were observed between dactylitis or LEI scores and other clinical outcomes.

Conclusion: In PsA pts with dactylitis or enthesitis at W0, GUS improved dactylitis or LEI scores vs PBO by W8; treatment differences were significant at W16 & W24. Resolution of dactylitis or enthesitis was significantly associated with clinically meaningful improvements in PsA joint & skin symptoms. Improved dactylitis scores correlated with improved skin symptoms and mental health; improved LEI scores correlated with improved physical function.

References:

- Deodhar A (A#807).
- Mease P (A#L13), Arthritis Rheumatol 2019;71(suppl 10);
- DOI: 10.1186/s13075-017-1399-5; DOI: 10.1016/j.semarthrit.2018.02.002

Table. Pooled DISCOVER-1&2: associations between dactylitis/enthesitis resolution and joint/skin response

		ACR20	ACR50	ACR70	PASI75 ^a	PASI90 ^a
Dactylitis resolution ^b	N	%pts	%pts	%pts	N	%pts
Q4W	373	55*	34*	16*	121	78*
Q8W	375	53*	31*	16*	116	80*
PBO	372	26*	12*	5*	115	19*
Enthesitis resolution ^c	N	%pts	%pts	%pts	N	%pts
Q4W	243	34*	31*	11*	187	82*
Q8W	230	40*	7*	12*	162	77*
PBO	255	14*	13*	5*	182	19*

* $p < 0.001$ (Chi-square)

^a In pts with $\geq 3\%$ BSA psoriasis & IGA ≥ 2 at W0

^b In pts with D at W0

^c In pts with E at W0

Fig. Pooled DISCOVER-1&2 LS mean changes from baseline over time in A) dactylitis and B) LEI scores

Acknowledgments: None

Disclosure of Interests: Dennis McGonagle Grant/research support from: Janssen Research & Development, LLC, Iain McInnes Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Atul Deodhar Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shelly Kafka Employee of: Janssen Scientific Affairs, LLC, Chetan Karyekar Shareholder of: Johnson & Johnson, Consultant of: Janssen, Employee of: Janssen Global Services, LLC. Previously, Novartis, Bristol-Myers Squibb, and Abbott Labs., Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Prasheen Agarwal Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Bei Zhou Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Christopher T. Ritchlin Grant/research support from: UCB Pharma, AbbVie, Amgen, Consultant of: UCB Pharma, Amgen, AbbVie, Lilly, Pfizer, Novartis, Gilead, Janssen, Proton Rahman Grant/research support from: Janssen and Novartis, Consultant of: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, and Pfizer., Speakers bureau: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer
DOI: 10.1136/annrheumdis-2020-eular.836